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ORIGINAL ARTICLE

Nasal carriage rate of *Staphylococcus aureus* among patients with systemic lupus erythematosus and its correlation with disease relapse

Mehrzad Hajialilo [a,*], Amir Ghorbanihaghjo [b], Alireza Khabbazi [a], Hamed Valizadeh [a], Sina Raeisi [b], Alka Hasani [a], Mojtaba Varshochi [a], Sousan kolahi [a], Mohamad Reza Nakhjavani [a]

[a] *Connective Tissue Diseases Research Center, Tabriz University of Medical Sciences, Tabriz, Iran*
[b] *Biotechnology Research Center, Tabriz University of Medical Sciences, Tabriz, Iran*

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KEYWORDS

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Abstract *Introduction:* Systemic lupus erythematosus (SLE) is an autoimmune disease with unknown origin. The disease causes a broad spectrum of signs and symptoms in a majority of body organs. Due to several factors like damage to mucosal surfaces and defect in complement systems, these patients are at a great risk of infections with opportunistic pathogens.

Aim of the work: To evaluate the nasal carriage of *Staphylococcus aureus*, rate of Methicillin-resistant *S. aureus* (MRSA) and its correlation with relapse in lupus patients.

Patients and methods: In an analytical-descriptive study, 80 patients (65 female and 15 male) with SLE attending the rheumatology clinics of Tabriz University of medical sciences were selected. Nasal mucosa specimens of the patients were taken and incubated in appropriate culture environment. All of the patients were followed for 1 year and the relapse of the disease was evaluated.

Results: The mean age of the patients was 25.35 ± 5.87 years. The mean disease duration was 3.66 ± 2.27 years and the mean SLE disease activity index (SLEDAI) was 6.40 ± 2.84. Thirty-nine out of 80 patients (48.75%) were positive for *S. aureus* in the nasal mucosa. Although no significant difference in SLEDAI was observed between the patients with nasal carriage of *S. aureus* and those without, the two groups were significantly different in the relapse and complement levels.

Conclusion: These results indicate that relapse of SLE in patients having *S. aureus* in their nasal mucosa is higher than in patients without.

* Corresponding author. Address: Connective Tissue Diseases Research Center, Tabriz University of Medical Sciences, Tabriz 51664, Iran. Tel.: +98 411 3363234; fax: +98 411 3363231.
E-mail address: hajialilo@gmail.com (M. Hajialilo).

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1. Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease with a prevalence of 20–150 in 100,000 which mainly affects young women in the range of 20–30 years [1,2]. Although the exact etiology of the disease is not clearly understood, it is thought to result from interplay of certain genetic factors, environmental factors and the infections such as Epstein–Barr virus (EBV) infection that is one of the suspected factors [3].

It has been shown that SLE patients are at high risk of different infections due to damage to mucosal surfaces, defect in the immune system with lymphocyte dysfunction, complement deficiency and spleen dysfunction as well as treatment with immunosuppressive agents. These factors can also contribute to disease relapse and hospitalizations of patients. The major cause of death in the first few years of illness is active disease (e.g., cerebritis, nephritis, or cardiovascular disease) and/or infection due to immunosuppression [4].

In some forms of vasculitis like Wegener's granulomatosis, the relationship between colonization of *Staphylococcus aureus* in the nasal cavity and disease relapse has been studied [5,6]. Some other studies have indicated the colonization of these bacteria in different parts of the body in patients with lupus. Nasal cavity colonization of these bacteria may lead to pneumonia by the same organisms. To the best of our knowledge, no study has been performed about the correlation between disease relapse and the colonization of these bacteria in patients with SLE. Previous studies have investigated the organism in oral microflora [7,8] and intestine [9].

The aim of the present study is to evaluate *S. aureus* colonization in SLE patients and their Methicillin-resistance and to study its correlation with disease relapse.

2. Patients and methods

This analytical-descriptive study was performed in the internal medicine department of Tabriz University of medical sciences, Tabriz, Iran. We enrolled 80 patients with SLE referring to Sina and Emam Reza hospitals and Sheikholraies clinic of Tabriz in the years 2012–2013. SLE was diagnosed according to the Systemic Lupus International Collaborating Clinics (SLICC) Classification Criteria [10].

The exclusion criteria were the anti-Staphylococcus therapy in the past 1 month, and the immune deficiency related conditions like diabetes, renal failure, IV drug abusing, cancers, organ transplantation and human immunodeficiency (HIV) infection. The ethics committee at the Tabriz University of Medical Sciences reviewed and approved the present study, in compliance with the Declaration of Helsinki. Informed consent was obtained from all participants.

At the beginning of the study all of the patients were completely examined and a blood sample was taken for assessment of the blood cell count, serum creatinine, anti-nuclear antibody (ANA), anti-ds DNA and complement levels as well as a urine sample for analysis.

The nasal sample was also obtained from the patients by a microbiologist and was cultured for 48 h in Mannitol salt agar environment after 16–20 h of incubation. Yellow colored colonies were evaluated initially with Disc Diffusion Oxacillin 1 μm, if the samples were resistant; they were tested with E-test for approving the MRSA. At the time of flares nasal culture was obtained again. The activity of SLE was evaluated using the SELENA SLE disease activity index (SLEDAI). Patients were followed up for 1 year and the flare was diagnosed as follows [11]:

Mild/moderate flare: a change in SLEDAI >3 points, or: new/worse skin, stomatitis, serositis, arthritis, fever, or increased prednisone <0.5 mg/kg/d, or added non-steroidal anti-inflammatory drugs (NSAIDs)/hydroxychloroquine, or >1.0 increase in a physician's global assessment (0–3 scale).

Severe flare: change in SLEDAI >12, or new/worse CNS-SLE, vasculitis, nephritis, myositis, platelet count $<60{,}000$, hemolytic anemia (Hb <7 mg/dl), requiring doubling or >0.5 mg/kg/d prednisone or hospitalization for SLE or new immunosuppressive, and/or increased physician's global assessment to >2.5.

All the information from the patients was recorded confidential and the patients could leave the study at the time of their decision.

Statistical evaluation was carried out with the SPSS 16.0 software (SPSS, Inc., Chicago, IL). Data obtained from the study groups were compared by Student's *t*-test and Mann–Whitney *U* test. A *p*-value <0.05 was regarded as statistically significant. All the results are expressed as mean ± standard deviation (SD).

3. Results

We studied 80 patients with SLE. Sixty-five patients (81.3%) were females and 15 (18.7%) were males. Demographic and clinical characteristics of patients are shown in Table 1.

Thirty-nine of the patients (48.72%) were carriers for *S. aureus* upon the nasal mucosa culture in Mannitol salt agar environment. From the 39 positive culture tests, 3 were resistant in Disc Diffusion Oxacillin test for which the E-test was done and all of them were sensitive.

Flare was seen at one year follow-up in 11 patients (13.75%). All of the flares were mild/moderate except for one severe flare in the *S. aureus* carriage group.

Both carriers and non-carriers of S. *aureus* did not differ significantly from each other regarding the SLEDAI, age and sex (Table 2). Hypocomplementemia was significantly more frequent in carriers ($p = 0.012$).

There was no significant association between the presence of renal involvement in carriers and non-carriers of S. *aureus* ($p = 0.012$) and recurrence had a significantly higher rate

Table 1 Systemic lupus erythematosus patients' demographic and clinical characteristics.

Number of patients (Female: Male)	80 (65:15)
	mean ± SD
Age (years)	25.35 ± 5.78
Disease duration (years)	3.66 ± 2.27
SLEDAI	6.4 ± 2.84
Treatment regimens N (%)	
HCQ + P	53 (66.25)
HCQ + P + CYC	23 (28.75)
HCQ + P + Cyclosporine	4 (5)

HCQ, hydroxychloroquin; P, prednisolone; CYC, cyclophosphamide.

Table 2 Characteristics of *S. aureus* carrier and non-carrier SLE patients.

Parameters	Carriers of *S. aureus* ($n = 39$)	Non Carriers of *S. aureus* ($n = 41$)	*p* value
Sex *N* (%)			
Female	32(18.1)	33(80.5)	NS
Male	7(17.9)	8(19.5)	NS
Hypocomplementemia	31(79.5)	12(29.3)	0.012
SLEDAI	5.4	6.4	NS
Flare during study	8 (20.5)	3 (7.3)	0.024
Mean time to flare from beginning of study (months)	2.95 ± 1.46	3.12 ± 1.32	0.043
Types of flare			
Mild/Moderate	7	3	NS
Severe	1	0	NS

NS, non significant.

among the carrier patients ($p = 0.024$) (Table 2). The mean time to recurrence in patients carrying *S. aureus* was significantly shorter than non-carrier patients ($p = 0.043$). The mean SLEDAI in patients with recurrence was 5.45 ± 2.34 and in patients without recurrence was 4.76 ± 2.56, which were not significantly different from each other ($p = 0.221$).

The correlation between the disease duration and *S. aureus* carrying was found to be significant, so the carrier rate increased with the increase in duration of the disease ($R = 0.566$).

Ten (4.24%) of non-carriers of *S. aureus* and 17 (6.43%) patients of carriers were on immunosuppressive drugs and there was no significant relation between immunosuppressive therapy and *S. aureus* carrying ($p = 0.57$).

4. Discussion

Systemic lupus erythematosus (SLE) is an autoimmune multisystemic disease producing autoantibodies against different parts of the body. Infections are a common complication and a major cause of death in all stages of SLE. Although infectious agents are known to trigger lupus disease expression and activity, the risk of different infections also is high in such patients [12]. Relapse of the disease is one of the major problems in the course of this illness.

Although etiologies of these relapses are not known, it seems that infections have a significant role in this matter.

Chen et al. recently reported that in Taiwanese patients with SLE, *S. aureus* was the most common Gram-positive bacteremia and nontyphoidal Salmonella and *Escherichia coli* were the most common Gram-negative pathogens isolated bacteria [13]. Gulneva et al. showed that in the intestine of patients with SLE, there was a significant increase of Staphylococcus and opportunistic *Enterobacteriaceae* detection rate [9].

The rate of carrying *S. aureus* in patients with SLE and the resistance for Methicillin and its relationship with the relapse of the disease were the main objectives of present study. Most of the current patients were categorized as having mild and moderate disease activity and only a small number of patients had a severe disease.

In the current study, the *S. aureus* rate of carrying was 48.72% which is more compared to the results of another study [14]. This study showed for the first time in an Iranian population that no MRSA cases were seen in patients with lupus and this is important in selection of the right antibiotic. The relapse of the disease was significantly higher in carriers while the disease activity, renal involvement, age and gender were not different. It seems that *S. aureus* carrying can show a higher rate of disease relapse. One major weakness is the small number of patients enrolled in the present study.

The reduction of the complements associated with the chance of carrying may reflect the role of complement system against the infections in patients of this study. We found that the longer the disease duration, the more the occurrence of carrying. The reason may be the decrease in complement levels, increase in hospitalization and the increase of colonization of *S. aureus* in such patients.

The immunosuppressive medications used in SLE of this study further contribute to susceptibility to infections. A prospective study of 110 lupus patients has shown that hypocomplementemia and a daily dose of prednisone greater than 20 mg for at least a month plus use of cyclophosphamide were significantly associated with infection [15]. In this study although 10 patients from 41 patients of non carrying and 17 patients from 39 patients of carrying *S. aureus* were on treatment with cyclophosphamide or cyclosporine, the differences between them were not statistically significant.

To our knowledge, this is the first study to report the relation of carrying *S. aureus* and relapse in patients with SLE in Iranian patients. Based on the results of our study, as well as data from other related studies, the rate of carriers of *S. aureus* in patients with SLE is higher compared with healthy subjects and the relapse of the disease is higher in such patients.

In conclusion, in patients harboring *S. aureus*, recurrence was significantly more common, whereas disease activity, renal involvement and age and gender differences were not significant. It can be concluded that the elimination of *S. aureus* from nasal cavity can reduce recurrence. But to establish this theory we need to conduct another study for the comparison of relapse with or without elimination of *S. aureus* in patients with lupus.

Conflict of interest

None.

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